CLAIMS

1. A method for identifying a compound for use in modulating, for example promoting, the activation or phosphorylation of AMPK (AMP-activated protein kinase) or AMPK subfamily member in a cell, the method comprising the steps of (1) determining whether a test compound modulates, for example promotes, the protein kinase activity of LKB1 and (2) selecting a compound which modulates, for example promotes, the protein kinase activity of LKB1.
2. The method of claim 1 wherein the LKB1 is in a preparation with STRAD and/or MO25.
3. The method of claim 1 or 2 wherein the LKB1, STRAD or MO25 is recombinant.
4. A purified preparation comprising LKB1, STRAD and recombinant MO25.
5. The preparation of claim 5 comprising recombinant LKB1.
6. The preparation of claim 4 or 5 comprising recombinant STRAD.
7. A cell capable of expressing LKB1, STRAD and overexpressed or recombinant MO25.
8. The cell of claim 7 comprising a recombinant nucleic acid encoding MO25.
9. The cell of claim 7 or 8 comprising a recombinant nucleic acid encoding LKB1.
10. The cell of any one of claims 7 to 9 comprising a recombinant nucleic acid encoding STRAD.

11. A cell comprising LKB1, STRAD and overexpressed or recombinant MO25.
12. A cell according to claim 11 comprising recombinant LKB1.
13. A cell according to claim 11 or 12 comprising recombinant STRAD.
14. A cell according to any one of claims 11 to 13 wherein the cell is a cell according to any one of claims 7 to 10.
15. A method for making a preparation according to any one of claims 3 to 6 comprising the step of purifying the preparation from a cell according to any one of claims 11 to 14.
16. A preparation obtainable by the method of claim 15.
17. The preparation of any one of claims 3 to 6 or 16 wherein the LKB1:STRAD:MO25 ratios are 1:1:1.
18. The method of claim 1, 2 or 3 wherein the LKB1 is in a preparation as defined in any one of claims 3 to 6 or 17 or a preparation obtained by or obtainable by the method of claim 15 or in a cell as defined in any one of claims 7 to 14.
19. The preparation or method of any one of claims 1 to 6, 15 to 18 wherein the preparation comprises a complex comprising the LKB1, STRAD and MO25.
20. A method for identifying a compound for modulating cellular LKB1 activity, the method comprising the steps of (1) determining whether a test compound modulates the LKB1 protein kinase activity of a preparation or complex as defined in any one of claims 3 to 6, 16, 17 or 19 claim 19 or in a cell as defined in any one of claims 7 to 14 and (2) selecting a compound which modulates the said LKB1 protein kinase activity.
21. The method of claim 1 or claim 20 wherein the LKB1 protein kinase activity is measured using AMPK or AMPK subfamily member or a fragment either thereof as the substrate.

22. A kit of parts comprising LKB1 or a recombinant polynucleotide encoding LKB1, STRAD or a recombinant polynucleotide encoding STRAD, and MO25 or a recombinant polynucleotide encoding MO25.

23. A kit of parts comprising (1) AMPK or AMPK subfamily member, or recombinant polynucleotide encoding AMPK or AMPK subfamily member or a fragment thereof and (2) a kit of parts as defined in claim 22 or a preparation or complex as defined in any one of claims 3 to 6, 16, 17 or 19 claim 19 or a cell as defined in any one of claims 7 to 14.

24. A method for overexpressing LKB1 comprising the steps of (1) selecting a cell type in which to overexpress LKB1, comprising the step of determining whether the cell type is one that expresses STRAD and/or MO25 (2) overexpressing LKB1 in the selected cell type.

25. A method for preparing LKB1 comprising the steps of (1) overexpressing LKB1 in a cell using a method according to claim 24 and (2) preparing LKB1 from the cell.

26. A method for identifying a putative binding partner for MO25 comprising the steps of (1) providing an amino acid sequence of at least the C-terminal three amino acids of a test putative binding partner (2) selecting a putative binding partner having the C-terminal amino acid sequence Trp-Glu/Asp-Phe.

27. The method of claim 26 further comprising the step of determining that the selected putative binding partner binds to MO25.

28. A method for identifying a genetic difference associated with PJS (Peutz-Jeghers Syndrome) comprising the steps of (1) investigating the sequence of a gene encoding a STRAD or MO25 isoform in at least one patient having PJS (2) identifying any difference between the said patient sequence and equivalent sequence from an individual without PJS.

29. A method for determining whether an individual is susceptible to PJS comprising the steps of determining whether the test individual has a genetic difference identified as associated with PJS by a method according to claim 28.

30. A method for identifying a compound which activates AMPK or AMPK subfamily member by a similar mechanism to metformin or phenformin or AICA riboside in which the effect of a test compound on the activation of AMPK or AMPK subfamily member by a preparation or complex as defined in any one of claims 3 to 6, 16, 17 or 19 claim 19 or a cell as defined in any one of claims 7 to 14 is compared with the effect of metformin or phenformin or AICA riboside on the activation of AMPK or AMPK subfamily member and a compound with a similar effect is selected.

31. Use of an AMPK subfamily member or polynucleotide encoding an AMPK subfamily member in the manufacture of a medicament for treating diabetes or obesity.

32. The method of any one of claims 1, 21 or 30, kit of parts of claim 23, or use of claim 31 wherein the AMPK subfamily member is or comprises an AMPKα1 or AMPKα2 polypeptide.

33. The method of any one of claims 1, 21, 30, kit of parts of claim 23 or use of claim 31 wherein the AMPK subfamily member is or comprises a NUAK1, NUAK2, BRSK1, BRSK2, SIK, QIK, QSK, MARK1, MARK2, MARK3, MARK4 or MELK polypeptide.

34. A peptide substrate for LKB1 comprising the amino acid sequence LSNLYHQGKFLQTFCGSPLY or FGNFYKSGEPLSTWCGSPPY or LSNMMSDGEFLRTSCGSPNY or MASLQVGDSLLETSCGSPHY or FSNEFTVGGKLDTFCGSPPY or AKPKGNKDYHLQTCCGSLAY; or a said sequence with from one to four substitutions therein at any position other than the underlined residue and/or a conservative

substitution at the underlined residue; or at least ten contiguous residues of a said sequence encompassing the underlined residue.

35. A peptide substrate for LKB1 consisting of the amino acid sequence LSNLYHQGKFLQTFCGSPLY or LSNLYHQGKFLQTFCGSPLYRRR or SNLYHQGKFLQTFCGSPLY or SNLYHQGKFLQTFCGSPLYRRR or LSNLYHQGKFLQTFCGSPLY or LSNLYHQGKFLQTFCGSPLYRRR or FGNFYKSGEPLSTWCGSPPY or FGNFYKSGEPLSTWCGSPPYRRR or LSNMMSDGEFLRTSCGSPNY or LSNMMSDGEFLRTSCGSPNYRRR or MASLQVGDSLLETSCGSPHY or MASLQVGDSLLETSCGSPHYRRR or FSNEFTVGGKLDTFCGSPPY or FSNEFTVGGKLDTFCGSPPYRRR or AKPKGNKDYHLQTCCGSLAY or AKPKGNKDYHLQTCCGSLAYRRR.

36. An antibody reactive with a peptide antigen having the amino acid sequence MVAGLTLGKGPESPDGDVS (residues 1-20 of human BRSK1), LSWGAGLKGQKVATSYESSL (residues 655-674 of human BRSK2), MEGAAAPVAGDRPDLGLGAPG (residues 1-21 of human NUAK1), TDCQEVTATYRQALRVCSKLT (residues 653-673 of human NUAK2), MVMADGPRHLQRGPVRVGFYD (residues 1-21 of human QIK), MVIMSEFSADPAGQGQGQQK (residues 1-20 of human SIK), GDCEMEDLMPCSLGTFVLVQ (residues 765-784 of human SIK), TDILLSYKHPEVSFSMEQAGV (residues 1349-1369 of human QSK), SGTSIAFKNIASKIANELKL (residues 776-795 of human MARK1), MSSRTVLAPGNDRNSDTHGT (residues 1-20 of human

MARK4), MKDYDELLKYYELHETIGTG (residues 1-20 of human MELK), CTSPPDSFLDDHHLTR (residues 344-358 of rat AMPKα1), CDPMKRATIKDIRE (residues 252 to 264 of rat AMPKα1).

37. A mutated AMPK subfamily member wherein the T-loop threonine residue corresponding to Thr172 of AMPKα1 is mutated to an alanine residue or to an aspartate or glutamate residue.

38. The mutated AMPK subfamily member of claim 37 wherein the AMPK subfamily member is BRSK1, BRSK2, NUAK1, NUAK2, QIK, SIK or MELK.

39. A polynucleotide encoding a mutated AMPK subfamily member according to claim 37 or 38.